# GOLD 2023: Implications for primary care of patients with COPD in the UK

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**In this article we review the major changes in the 2023 GOLD report as they impact on the initial and ongoing pharmacological management of COPD and consider the implications for primary care in the UK. Dr Fiona Mosgrove is a GP in Aberdeen and Clinical Lead for the Grampian Respiratory Improvement Programme. Dr Tracey Lonergan is the Policy Coordinator for the Primary Care Respiratory Society and Medical Writer with a special interest in respiratory disease.**

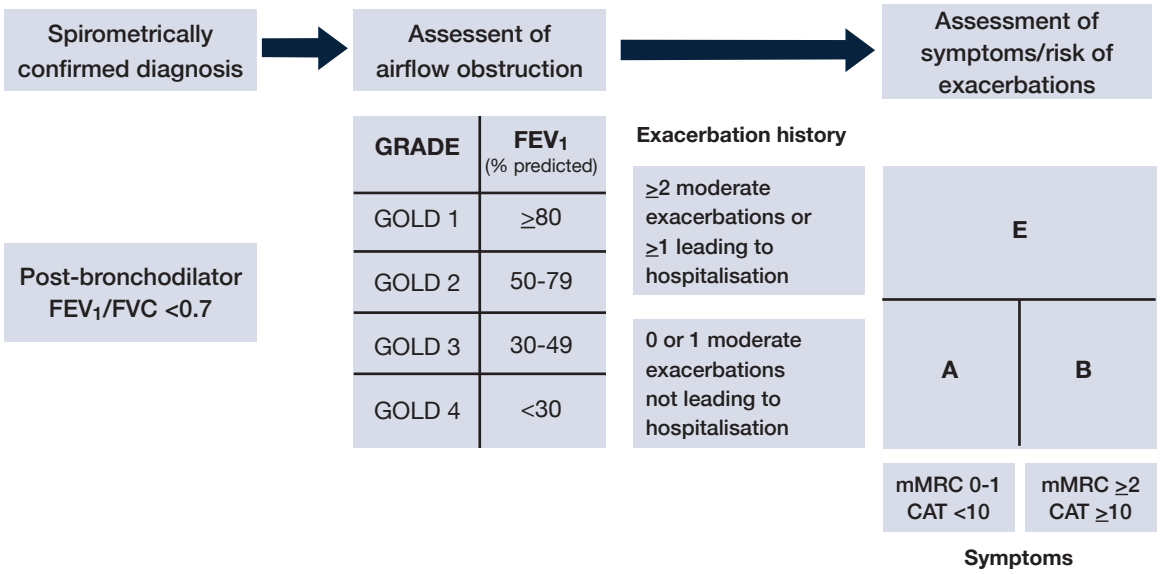
## Background

Chronic obstructive pulmonary disease (COPD) is the second most common lung disease in the United Kingdom.[1] An estimated 2.2% of the adult population are living with a diagnosis of COPD in 2022, equating to more than 1.2 million people.[1] While the prevalence of COPD in the UK is comparable to that of other European countries, we have the 3rd highest mortality rate from the disease.[1,2] These figures are a stark reminder that we still have some way to go to improve the lives and outcomes of people diagnosed with COPD in the UK.

Over the past decade, the UK has been playing catch up in terms of clinical guidelines for the diagnosis and management of COPD. In an attempt to address this, from a primary care perspective, in 2017 the Primary Care Respiratory Society (PCRS) published a treatment algorithm for COPD in the UK focusing on the pharmacotherapeutic management aspect.[3] In 2018 the National Institute for Health and Care Excellence (NICE) issued updated guidance for the prevention, diagnosis, and management of COPD, the first major update since 2004.[4] Unfortunately, the 2018 revision omitted two key aspects of pharmacotherapy for COPD, the role of triple inhaled therapies and the duration of oral corticosteroid (OCS) treatment. Following a consultation process in 2018, these omissions were considered to be sufficiently significant to require an immediate update, with revised guidelines published in 2019.[5] In contrast, reports from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) have been updated every 18–24 months over the past decade, adapting to emerging insights into the pathobiology of the disease and the results of clinical trials of new treatment options.[6] The latest GOLD report, issued in November 2022, includes a number of significant changes incorporating the results of recent longitudinal studies and Phase 3 drug trials.[6] These studies are changing how we view COPD at the most fundamental level and consequently how we approach the treatment of patients.

In this article, we review the major changes in the 2023 GOLD report as they impact the initial and ongoing pharmacological management of COPD. We also consider the updated recommendations from NICE published in 2019 and whether our 2017 consensus guideline for the treatment of patients with COPD in the primary care setting remains relevant.

**Figure 1.** The GOLD ABE Assessment Tool[6]




CAT, COPD Assessment Test; MRC, Medical Research Council; $FEV_1$, forced expiratory volume over 1 second; FVC, forced vital capacity.



## 2023 GOLD guidelines

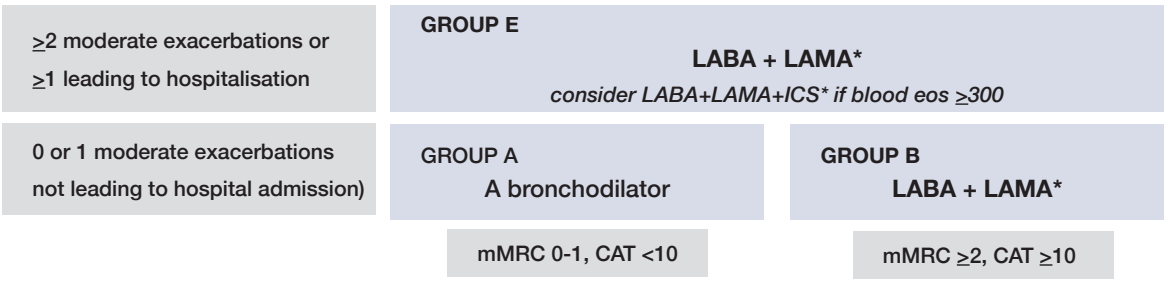
### Assessment and classification of COPD

The latest GOLD guideline includes a major change in the way COPD is assessed and classified.[6] The GOLD Refined Assessment Tool, first introduced in 2017, included spirometric assessment of airflow obstruction and grouping of patients based on symptoms (primarily breathlessness) and recent history of exacerbations (as an indicator of future exacerbation risk). The original model stratified patients into four groups (A, B, C and D) based on high or low exacerbation risk and high or low symptoms. Initial pharmacological treatment was determined on the basis of these groupings. The recommendation for patients with a low exacerbation risk was a bronchodilator for those with a low symptom burden (Group A) and a long-acting bronchodilator (LABA or long-acting muscarinic agent [LAMA]) for those with a high symptom burden (Group B). For patients with a high exacerbation risk, a LAMA was recommended for those with a low symptom burden (Group C) with combination therapy (LAMA + LABA or LABA + inhaled corticosteroid [ICS]) for those with a high symptom burden (Group D).

While the assessment of severity based on spirometric evaluation remains, the grouping of patients by symptom burden and future exacerbation risk has changed in the 2023 update (Figure 1) along with the recommended initial pharmacotherapy for each group (Figure 2).[6]

**Management of patients with a low risk of future exacerbations**. While treatment for patients with a low exacerbation risk and low symptom burden (Group A) remains the same, a

**Figure 2.** Initial pharmacological treatment of COPD[6]




* single inhaler therapy may be more convenient and effective than multiple inhalers

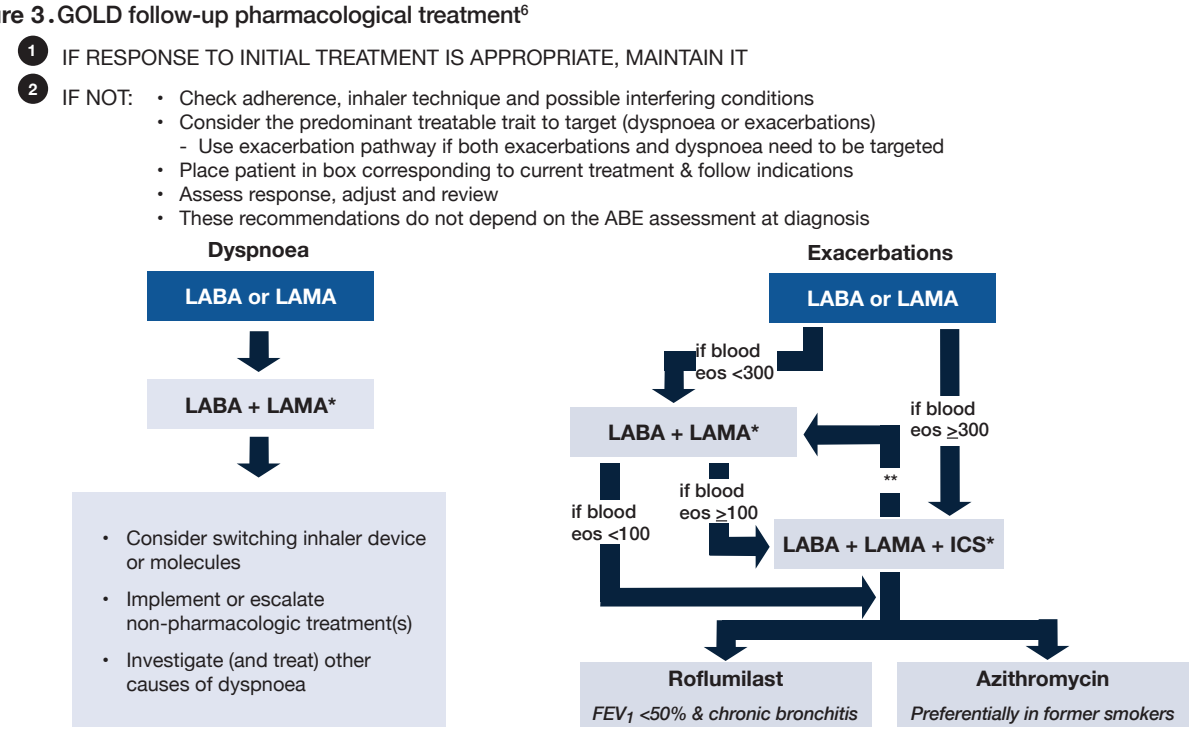
CAT, COPD Assessment Test; ICS, inhaled corticosteroid; LABA, long-acting bronchodilator; LAMA, long-acting muscarinic agent; MRC, Medical Research Council.

monotherapy approach has been abandoned for patients with a low exacerbation risk and high symptom burden (Group B).[6] For these patients, the initial treatment should be LABA + LAMA combination therapy, preferably in a single inhaler. These recommendations are based on the results of Phase 3 clinical trials of several LABA/LAMA combinations which consistently demonstrated improved lung function and health-related quality of life compared with either agent alone and also when compared with a LABA + ICS regimen.[7] Indeed, the 2023 report is very clear that there is no longer a role for the LABA + ICS combination for the initial treatment of patients with COPD at low risk for exacerbations.

**Management of patients with a high risk of future exacerbations**. Perhaps the most significant change is that patients at high risk for exacerbations are no longer stratified by symptom burden.[6] Instead, these patients are grouped together as Group E, with initial treatment being a LABA + LAMA combination (Figure 2). For these patients, a more rational approach to ICS use is recommended, guided by clinical factors and blood eosinophil levels. Patients that are unlikely to benefit from an ICS are those with a blood eosinophil count <100 cells/µL. ICS therapy can be considered for patients with a blood eosinophil count between 100 and <300 cells/µL who have had one moderate COPD exacerbation in the previous year. Patients most likely to benefit from ICS therapy are those with a blood eosinophil count >300 cells/µL, a history of hospitalization for COPD exacerbations, ≥2 moderate exacerbations a year or with a history of, or concomitant asthma. When considering starting an ICS, blood eosinophils are not the only useful factor. There are known harms of ICS use, including an increased risk of pneumonia and of mycobacterial infection. Patients with a history of recurrent pneumonia and those with a previous mycobacterial infection should not routinely be started on ICS as the harms may well outweigh the benefits. These fundamental changes to the classification and initial treatment of patients with a high risk of future exacerbations reflect the findings of the ECLIPSE study. This study showed that eosinophil count, an indicator of underlying inflammation, was a better predictor of response to ICS therapy than was a high symptom burden.[8]

**Management of patients with ongoing symptoms or exacerbations.** The rational approach to the use of ICS therapy based on evidence of an underlying inflammatory process, greatly simplifies both the approach to initial treatment and the follow-up treatment decisions (Figure 3).[6] The first step for any

**Figure 3. GOLD follow-up pharmacological treatment[6]**




* single inhaler therapy may be more convenient and effective than multiple inhalers

** Consider de-escalation of ICS if pneumonia or other considerable side effects. In case of blood eos ≥300 cells/µl de-escalation is more likely to be associated with the development of exacerbations

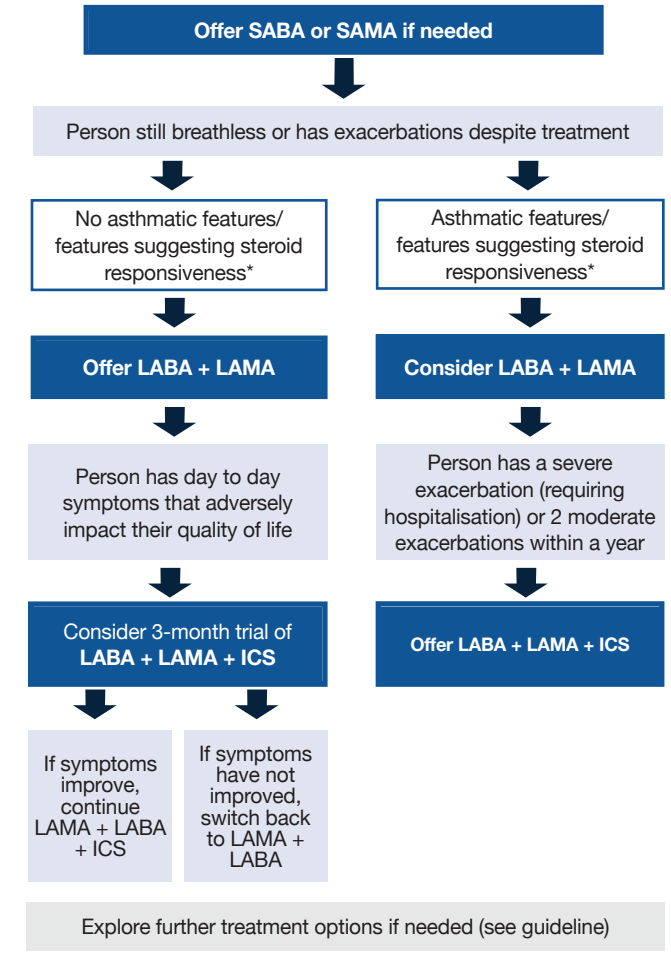
CAT, COPD Assessment Test; eos, eosinophils; FEV1, forced expiratory volume over 1 second; ICS, inhaled corticosteroid; LABA, long-acting bronchodilator; LAMA, long-acting muscarinic agent; MRC, Medical Research Council.

patients with ongoing symptoms or repeated exacerbations is to review and optimise their current treatment regimen – check inhaler technique, consider whether any comorbid conditions are present or require review. Next steps depend on whether the patients has ongoing breathlessness or repeated exacerbations, regardless of their initial grouping.

Patients with ongoing breathlessness who were receiving bronchodilator monotherapy can be escalated to combination LABA + LAMA therapy.[6] For those already on combination therapy, switching to an alternative device or molecule can be considered alongside a focus on treatment optimisation, non-pharmacological management, and investigation of alternative causes of breathlessness.

Patients with ongoing exacerbations can be escalated to triple therapy including an ICS if elevated eosinophils to >300 cells/μL, or to roflumilast (for those with an $FEV_1$ <50% and chronic bronchitis) or azithromycin (preferentially in former smokers).[6] However, the reliance on elevated blood eosinophils as the single biomarker for ICS initiation in exacerbating patients has its critics, not least because the question remains as to when to assess for eosinophils as a patient with a recent exacerbation who has received oral steroids (prescribed or via their emergency pack) may not meet the 300 cells/μL cut-off.

**Figure 4. NICE inhaled therapies algorithm[5]**




* Asthmatic features/features suggesting steroid responsiveness in this context include any previous secure diagnosis of asthma or atopy, a higher blood eosinophil count, substantial variation in $FEV_1$ over time (at least 400ml) or substantial diurnal variation in peak expiratory flow (at least 20%)

## 2019 NICE guidelines

So where are we with our UK guidelines? Initial therapy for all patients with COPD remains single bronchodilator therapy with a short-acting bronchodilator (SABA) or short-acting muscarinic antagonist (SAMA) (Figure 4).[5] Patients limited by symptoms or exacerbations can then be treated more aggressively if asthmatic features are present.

Patients with asthma symptoms or exacerbations can then be treated more aggressively if asthmatic features are present.[5] This is the first and major difference from the 2023 GOLD guidelines. Whereas GOLD focuses on symptoms and future exacerbation risk as the 'treatable traits' guiding pharmacotherapeutic decision making, NICE has continued to focus on the presence of asthmatic features as the main 'treatable trait'.

**Management of patients with asthmatic features**. For patients with features suggestive of an asthmatic component (secure diagnosis of asthma or atopy, higher blood eosinophil count, substantial variation in FEV1 over time or substantial diurnal variation in peak expiratory flow), a combination LABA + LAMA can be considered.[5] A limitation here is that the cut-off for 'higher eosinophil count' is not specified although it is generally accepted as >300 cells/μL. Triple therapy with the addition of ICS can subsequently be offered for patients who experience a severe exacerbation (requiring hospitalization) or who experience 2 moderate exacerbations within a year.

**Management of patients without asthmatic features**. Patients without asthmatic features can be offered a LABA + LAMA and, if symptoms continue to impact their quality of life, a 3-month trial of triple therapy with LABA + LAMA + ICS can be considered.[5] This approach differs from the 2023 GOLD report as it still allows for a trial of treatment with ICS even in the absence of a single point of evidence of underlying inflammation – blood eosinophils >300 cells/μL required by GOLD.

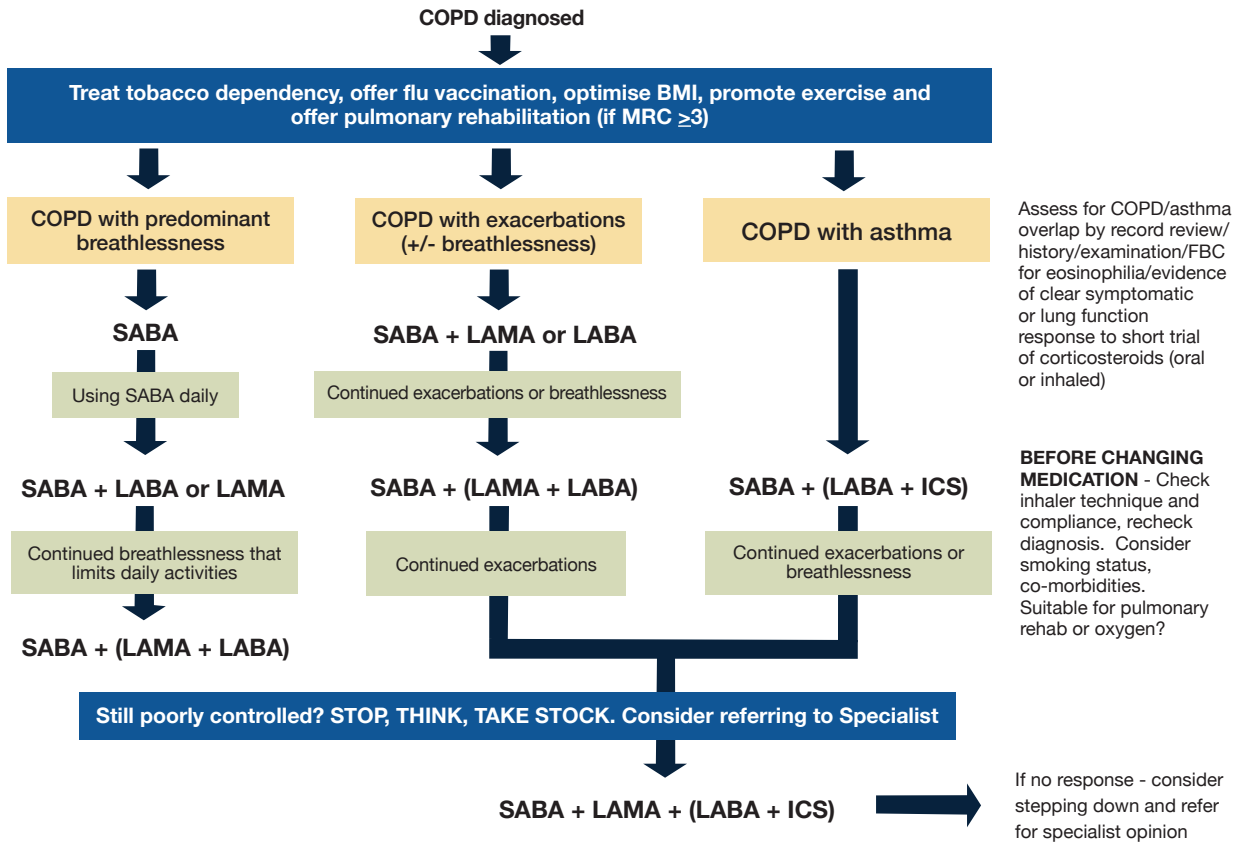
Unfortunately, the 2019 update did not address the concern

around including an option for a 3-month trial of triple therapy for patients with ongoing breathlessness but no evidence of an increased risk for future exacerbations. As we have seen from the ECLIPSE study, ongoing breathlessness is not a good indicator for response to ICS therapy and it was for this reason that the 2023 GOLD update elected to require elevated eosinophils as a marker of underlying inflammation as a pre-requisite for ICS initiation.[6] Allowing triple therapy as an option for patients with ongoing breathlessness is concerning as it is unlikely to prove benefit in relieving their breathlessness and may cause a delay in seeking alternative causes for their chronic breathlessness. This approach will mean that a proportion of patients will be escalated to triple therapy and receive an ICS from which they will gain no clinical benefit and which may place them at increased risk for pneumonia. While the NICE 2019 update recommends that patients whose symptoms do not improve after a 3-month trial of triple therapy should step down to a dual bronchodilator regimen without an ICS, whether this is feasible and currently part of routine practice is unclear.

## PCRS 'Keeping it Simple' approach

In 2017, PCRS issued their consensus guidance on the management of patients with COPD in the context of UK primary care (Figure 5).[3] Indeed, the recent updates to the GOLD and NICE guidance reflect the approach, laid out in the 2017 document, to initial and follow-up pharmacological management of COPD. Our guidance on treatment decision-making considers the treatable traits targeted in the 2023 GOLD guidance – breathlessness and exacerbations – as well as the asthmatic component targeted in the NICE guidance. Three treatment pathways reflect the different clinical needs and likely underlying pathology associated with these treatable traits. Patients with an asthmatic component are likely to benefit from ICS and this should form a part of their initial treatment regimen. Patients with breathlessness as their major clinical feature and without asthma will not benefit from ICS therapy and their treatment should focus on bronchodilation, SABA, LABA or LABA + LAMA depending on the impact of their breathlessness on their daily activities. Patients who are exacerbating can start on a SABA in addition to single agent

**Figure 5.** PCRS 'Keeping it Simple' approach[3]



bronchodilation with a LAMA or LABA. If breathlessness is still impacting activities of daily living then dual long-acting bronchodilator therapy (LABA + LAMA) can be commenced. ICS (triple therapy) can be used in addition to dual bronchodilation if they continue to experience exacerbations. At each stage, medication optimisation should be undertaken including checking the patient's inhaler technique and their adherence. In addition, ongoing monitoring of patients should include reviewing for comorbidities (especially alternative causes of breathlessness) and whether pulmonary rehabilitation has been offered and attended as well as treating tobacco dependency and offering appropriate vaccinations.

## Conclusions

Overall, both GOLD and NICE appear to be catching up with the pragmatic recommendations PCRS made in 2017. Steroid stewardship, both OCS and ICS, remains relevant to avoid exposing patients to treatments that will not benefit them and which may in fact place them at risk for side effects. Looking back over the last decade, we have come a long way in our understanding of the heterogeneity of COPD and this has informed how best to manage patients according to the treatable traits that are most significant for them. While a cure for COPD remains elusive and treatment is largely reactive to clinical presentation, there is much we can do to ensure patients receive treatments that relieve their most impactful daily symptoms, optimise their lung function and reduce their risk for life-threatening exacerbations.

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